In the Claims:

Please cancel claims 63-71 in response to the restriction requirement.

Claims 1-56 (canceled).

57. (Currently amended) A method for directing the biosynthesis of specific polyketide analogs by genetic manipulation of a polyketide-producing microorganism, said method comprising the steps of:

(1) isolating a polyketide biosynthetic gene-containing DNA sequence;

(2) identifying within said gene-containing DNA sequence, a sequence fragment ~~polyketide synthase domain~~ encoding for polyketide synthase ~~for an~~ enzymatic activity;

(3) introducing one or more specified changes into said ~~polyketide synthase domain~~ sequence fragment resulting in an altered DNA sequence;

(4) introducing said altered DNA sequence into a polyketide-producing microorganism to replace an original sequence;

(5) growing a culture of the altered microorganism under conditions suitable for the formation of the specific polyketide analog; and

(6) isolating said specific polyketide analog from the culture.

58. (Currently amended) The method of claim 57 wherein said polyketide synthase enzymatic ~~activities comprise~~ activity is selected from the group consisting of β-ketoreductase, dehydratase, acyl carrier protein, enoylreductase, β-ketoacyl ACP synthase, and acyltransferase.

59. (Original) The method of claim 57 wherein said alteration which occurs in the DNA sequence results in the inactivation of one or more enzymatic activities involved in the processing of the β-carbonyl of said polyketide.

60. (Currently Amended) The method of claim 59 wherein said inactivated enzymatic ~~activities affecting~~ activity is involved in the processing of β-carbonyl of said polyketide and said inactivated enzymatic activity is selected from the group consisting of ~~the~~ β-ketoreductase, dehydratase, and enoylreductase.

61. (Original) The method of claim 59 wherein said alteration in the DNA sequence results in the addition of one or more enzymatic activities involved in the β-carbonyl processing of said polyketide.

62. (Original) The method of claim 61 wherein said additional enzymatic activities are selected from the group consisting of β-ketoreductase, β-ketoreductase and dehydratase, and β-ketoreductase, dehydrataseand enoylreductase.

Claims 63-71 (canceled).

72. (Original) The method of claim 57 wherein said DNA sequence is isolated from a species of the *Actinomycetales* family.

73. (Previously Amended) The method of claim 72 wherein said DNA sequence is isolated from a genus selected from the group consisting of *Actinomyces, Dactylosporangium, Micromonospora, Nocardia, Saccharopolyspora, Streptoverticillium*, and *Streptomyces*.

74. (Original) The method of claim 73 wherein said genus is selected from the group consisting of *Saccharopolyspora* and *Streptomyces*.

75. (Original) The method of claim 74 wherein said genus is *Saccharopolyspora* and the species is *erythraea*.

76. (Original) The method of claim 74 wherein said genus is *Saccharopolyspora* and the species is *hydroscopicus*.

77. (Previously Amended) The method of claim 57 wherein said polyketide is selected from the group consisting of macrolides, tetracyclines, polyethers, polyenes, ansamycins and derivatives or analogs thereof.

78. (Original) The method of claim 77 wherein said polyketide is a macrolide.

79. (Original) The method of claim 78 wherein said macrolide is an erythromycin.

80. (Original) The method of claim 79 wherein said erythromycin is selected from the group consisting of 11-oxo-11-deoxyerythromycin A, 7-hydroxyerythromycin A, 6-deoxy-7-hydroxyerthythromycin A, 7-oxoerythromycin A, 3-oxo-3-deoxy-5-desoaminylerythronolide A, Δ-6,7-anhydroerythromycin A, ((14S, 15S)14(1-hydroxyethyl)erythromycin A, 11-epifluoro-15-noreythromycin A, 14-(1-propyl)erythromycin A, and 14[1(1-hydroxypropyl)]erythromycin A.

81. (Previously Amended) The method of claim 57 wherein said DNA sequence, designated *eryA*, encodes a protein having enzymatic activities associated with the formation of 6-deoxyerythronolide B.

82. (Previously Amended) The method of claim 57 wherein said gene-containing DNA sequence encodes one or more proteins having enzymatic activities in the rapamycin biosynthetic pathway.

83. (Currently Amended) The method of claim 57 wherein said polyketide <u>analog</u> is a rapamycin analog.

84. (New) A method for directing the biosynthesis of a specific polyketide analog by genetic manipulation of a polyketide-producing microorganism, wherein the method comprises the steps of:

(1) isolating a DNA sequence from a polyketide-producing microorganism encoding a polyketide synthase polypeptide comprising one or more domains providing enzymatic activities that support polyketide biosynthesis;

(2) identifying one or more regions of the DNA sequence encoding specific domains within the polyketide synthase polypeptide;

(3) altering the DNA sequence encoding the polyketide synthase polypeptide by either or both of,

(i) disrupting the DNA sequence encoding the polyketide synthase in one or more regions encoding a domain providing a β-carbonyl processing enzymatic activity selected from the group consisting of a β-ketoreductase, dehydratase, and enoylreductase, the disruption resulting in inactivation of said enzymatic activity in polyketide biosynthesis, and,

(ii) inserting within the DNA sequence encoding the polyketide synthase one or more DNA sequences encoding a domain providing β-carbonyl processing enzymatic activity selected from the group consisting of a β-ketoreductase, dehydratase, and enoylreductase, the insertion resulting in the addition of said enzymatic activity in polyketide biosynthesis;

(4) transforming a polyketide-producing microorganism with the altered polyketide synthase-encoding DNA sequence to replace its native polyketide synthase-encoding DNA sequence of the microorganism;

(5) culturing the transformed microorganism in conditions suitable for the expression of the altered polyketide synthase and the biosynthesis of a specific polyketide analog by the altered polyketide synthase; and

(6) isolating the specific polyketide analog from the cultured cells or the culture medium.